

REMARKS

Claims 1-10 and 12-18 are currently pending in this application.

In view of the amendment and the following remarks, Applicants respectfully request reconsideration and reexamination of this application and timely allowance of the pending claims. Claim 1 has been amended to merely add “a” before “first” and “second” in steps (b) and (c).

I. The Rejections Under 35 U.S.C. § 103(a) Should be Withdrawn

A. The Rejections

Claim 18 was rejected under 35 U.S.C. § 103(a) on page 3 of the Office Action as allegedly obvious over PCT International Application Number WO 97/27317 to Lockhart *et al.* (“Lockhart”) in view of U.S. Patent Number 5,700,637 to Southern (“Southern”).

Claims 1-10 and 12-18 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent Number 5,631,134 to Cantor (“Cantor”) in view of U.S. Patent Number 5,545,531 to Rava *et al.* (“Rava”).

Claims 1-10 and 12-18 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Cantor in view of U.S. Patent Number 5,807,522 to Brown *et al.* (“Brown”) and U.S. Patent Number 4,981,783 to Augenlicht (“Augenlicht”).

Applicants respectfully traverse the rejection for the following reasons.

B. The Relevant Case Law

The Federal Circuit has set forth three basic criteria that must be met to establish a case of *prima facie* obviousness. First, there must have been at the time of the invention a motivation to combine or modify the teachings of the references cited. *Ecolochem, Inc. v. Southern California Edison Company*, 227 F.3d 1361, 1372 (Fed. Cir. 2000) (holding obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention,

absent some teaching or suggestion supporting the combination); see also *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988) (holding that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art). Second, the alleged prior art must teach or suggest all of the limitations of the claims alleged to be obvious. *In re Royka*, 490 F.2d 488 (CCPA 1974) (holding that to establish *prima facie* obviousness of a claimed invention, all of the claim limitations must be taught or suggested by the prior art); *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991) (holding that the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure). Third, there must have been at the time of the invention a reasonable expectation of success. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-1208 (Fed. Cir. 1991), *cert. denied* 502 U.S. 856 (1991) (holding that obviousness requires references to show that there was, at the time of the invention, a reasonable expectation of success).

C. Applicants Response to the Rejections

1. The First Obviousness Rejection

Claim 18 was rejected on pages 3-4 of the Office Action under 35 U.S.C. § 103 as obvious over Lockhart (WO 97/27317) in view of Southern.

The Examiner is respectfully directed to the updated priority information in the amendment of November 17, 2004 where priority is claimed to Lockhart *et al.* (WO 97/27317). Accordingly, the Lockhart *et al.* PCT is not available as prior art and Applicants respectfully request that the rejection of claim 18 under 35 U.S.C. § 103 be withdrawn.

2. The Second Obviousness Rejection

Claims 1-10 and 12-18 were rejected on pages 4-7 of the Office Action under 35 U.S.C. §

103 as obvious over Cantor in view of Rava *et al.* As set forth in the Office Action, the Examiner recognizes that Cantor *et al.* “do not specifically teach hybridization to two arrays and comparison and signal normalization to determine the presence of a mutation” (Office Action at page 7, lines 4-6). The Examiner, however, suggests that Cantor “clearly suggests comparative hybridization because to determine a change in sequence (i.e. mutation) the sequence must be compared to an unchanged (wild-type) sequence” (Office Action at page 7, lines 1-3). The Examiner then finds that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the well known two array hybridization and signal comparison of Rava to the sequence analysis of Cantor based on Cantor’s desire to analyze sequences to diagnose mutations.

Applicants respectfully traverse the pending rejection. As recognized by the Examiner, the Cantor disclosure is directed to methods of sequencing by hybridization. The endpoint of the methods disclosed in Cantor is the construction of an actual sequence not a hybridization pattern that is compared to a reference hybridization pattern. For instance, see column 7, lines 16-24, where the disclosed sequencing by hybridization methods are described as lending themselves to “computer analysis and automation...for sequence reconstruction...” See also Example 14 where Cantor presents a discussion of automated methods of creating “contiguous sequence information from hybridization result[s.]” Cantor simply does not teach or suggest creating a target hybridization pattern and a reference hybridization pattern, normalizing the probe intensities and comparing the intensity differences to directly determine whether a mutation is present.

At page 7, lines 1-3 of the Office Action, the Examiner appears to rely on a statement in the Cantor disclosure that the “sequence must be compared to an unchanged (wild-type) sequence” to provide motivation to modify the sequencing methods of Cantor with the teachings of Rava *et al.* Careful reading of Cantor at the column and line numbers cited by the Examiner (column 4, lines 1-8 of Cantor) reveal that Cantor was referring to the sequencing methods and that any suggested comparison would be a sequence to sequence comparison, not the comparison

of hybridization patterns as required by the pending claims. The teachings of Rava *et al.* referred to by the Examiner have nothing to do with this prophetic disclosure of Cantor.

Applicants respectfully remind the Examiner that there must have been at the time of the invention a motivation to combine or modify the teachings of the references cited and that said motivation must found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See 227 F.3d at 1372. In this case, no motivation can be gleaned from the cited references to modify the teachings of Cantor. As set forth above, the methods of Cantor result in the construction of actual sequences and Cantor never suggests that target and reference hybridization patterns be produced. Given this complete disclosure with no suggestion of any deficiency or reason to modify Cantor's disclosure, the teachings of Rava *et al.* are not properly combinable to obviate the pending claims. The Examiner seems to acknowledge the incongruity between the teachings of Cantor and the teachings of Rava *et al.* in the statement "it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the well known two-array hybridization...of Rava to the sequence analysis of Cantor based on Cantor's desire to analyze sequences to diagnose mutations" (Office Action at page 7, lines 7-10). [Emphasis added.] Applicants respectfully submit that any comparison done using the teachings of Cantor would have been done at the actual determined sequence level, not by comparing target and reference hybridization patterns because even the combined teachings of Cantor and Rava do not provide the motivation to deviate from the sequence comparisons suggested in Cantor. As no *prima facie* case of obviousness has been made, Applicants request reconsideration and withdrawal of the pending rejection.

2. The Third Obviousness Rejection

As summarized above, claims 1-10 and 12-18 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Cantor in view of U.S. Patent Number 5,807,522 to Brown *et al.* and U.S.

Patent Number 4,981,783 to Augenlicht.

The teachings and deficiencies of Cantor are discussed above and Applicants respectfully submit that this discussion is also pertinent to this rejection under 35 U.S.C. § 103(a). Just as in the case of the combination of Cantor and Rava *et al.* discussed above, Brown *et al.* and Augenlicht do not provide any motivation, either singularly or in combination to modify the sequencing by hybridization methods of Cantor. The Office Action states that the motivation is “for the expected benefit of rapid and convenient mass screenings for diagnostic and prognostic applications...” (Office Action at page 9, lines 7-9). Applicants find no such motivation that would lead one of ordinary skill in the art to modify the sequencing methods of Cantor.

Concerning the Brown *et al.* reference, this patent discloses multi-array substrates. Augenlicht merely suggest methods of comparing hybridization patterns between a cloned sequence and a “known standard” to a cloned gene array to “determine the existence of malignant or premalignant tissue” (column 4, lines 18-23). Neither reference teaches or suggests why one of ordinary skill in the art would want to modify the sequencing methods of Cantor by these non-sequence-based methodologies. In fact, the whole purpose of the methods disclosed in Cantor is to arrive at a generation of contiguous sequence information (see column 3, lines 31-39 under “Summary of the Invention” and Example 14, column 18, lines 63-65) and modification of the disclosed methods with the teachings of Brown *et al.* and Augenlicht would not further the purpose of the methods of Cantor. Applicants respectfully submit that without a motivation derived from the prior art to modify the sequencing by hybridization methods of Cantor to arrive at the claimed invention, no *prima facie* case of obviousness has been made and the pending rejection should be withdrawn.

II. The Obviousness-Type Double Patenting Rejection Should be Withdrawn

A. The Rejections

Claims 1-10 and 12-18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 and 18 of U.S. Patent 6,344,316 to Lockhart *et al.*

B. Applicants Response to the Rejection

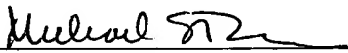
Applicants respectfully traverse and request that the pending rejection be withdrawn. The Office Action states that the pending claims and claims 1-4 and 18 of the '316 patent "merely differ in the in the arrangement of the limitations with the claim sets and the intended use of the method steps" (Office Action at sentence spanning pages 12 and 13). Instant claim 1, however, recites numerous limitations that distinguish the instant claims from the claims of the '316 patent. For instance, step (a) of instant claim 1 recites that each probe of the array comprises a double stranded region and a single stranded region. No such limitation is found in the claims of the '316 patent. Step (b) of instant claim 1 requires the hybridization of a target polynucleotide to overhang regions of the probes on the array. No such limitation is found in the claims of the '316 patent.

Applicants note that an obviousness-type double patenting rejection must be based on the obviousness standard of 35 U.S.C. 103(a). MPEP § 1504.06. No such determination is apparent from the Office Action and Applicants respectfully submit that withdrawal of the pending rejection is in order.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No.50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP



Michael S. Tuscan
Reg. No. 43,210

Dated: August 30, 2005
Morgan, Lewis & Bockius LLP
1111 Pennsylvania Ave., NW
Washington, DC 20004
Tel: 202.739.3000
Fax: 202.739.3001